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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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EXAMINER	
YU, MELANIE J	

ART UNIT	PAPER NUMBER
1641	

DATE MAILED: 07/19/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/017,437	RAO ET AL.	
	Examiner	Art Unit	
	Melanie Yu	1641	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *09 May 2005*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-11 and 15-17* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-11 and 15-17* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *18 December 2001* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

1. Applicant's amendment filed 9 May 2005 has been entered. Claims 1, 6, 7 and 15-17 are currently amended. Claims 12-14 are canceled. Claims 1-11 and 15-17 are pending in this application.

Withdrawn Rejections

2. Previous rejection of claims 1-11 under 35 USC 102(b) have been withdrawn in light of applicant's amendment.

Claim Rejections - 35 USC § 112

3. Claims 1-11 and 15-17 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Regarding claims 1 and 15, the term "optimized" is vague because it is unclear how the paramagnetic particles are optimized, what type of optimization is required and the amount of optimization encompassed by the term. The term "pre-coated" is vague because it is unclear whether the paramagnetic particles are pre-coated with a paramagnetic material, or whether the particle is pre-coated with another substance such as a second binding partner. It is unclear what physical limitations are required for the paramagnetic particle to be optimized and pre-treated. Claim 1 recites "the bound pre-coated paramagnetic particles" at line 12 of the claim, which is vague because it is unclear to what the paramagnetic particles are bound. It is unclear if the particles are bound to streptavidin, a first binding partner or a second binding partner. It is indefinite as to whether the streptavidin binding capacity recited in line 11 of claim 1 refers to a binding capacity of the paramagnetic particles or the non-magnetic particles. It is further unclear

whether the first binding partner operably linked with the non-magnetic microparticles recited in line 3 is the same first binding partner bound to pre-coated paramagnetic particles recited in line 15. It is unclear whether a first binding partner is bound directly to the non-magnetic microparticles or whether a first binding partner is bound to a non-magnetic microparticle indirectly through a second binding partner and a paramagnetic bead.

Claim 6 recites "capable of indirectly binding" which is vague because it is unclear whether the paramagnetic particles are actually bound to the at least three entities. It is further vague as to whether the three additional entities are being claimed or whether the particles must merely be capable of the recited indirect binding.

Regarding claim 7, it is unclear if the detectable labels are linked to the first binding partner of claim 1, or the detectable labels are linked to a different first binding partner. It is unclear if the additional entities listed are targets for binding or the additional entities are attached to the magnetic particle for the binding other targets.

Claim 15 recites "pretreated with paraformaldehyde" which is drawn to a method and does not appear to provide any further product limitations. It is unclear whether paraformaldehyde is being claimed as part of the composition and what physical limitations are provided by pretreatment with paraformaldehyde. Claim 15 further recites "bound to nonhaving a detectable fluorescent label" which is vague and indefinite. It is unclear whether the paramagnetic particles are bound to a detectable fluorescent label. The definition for the term "nonhaving" is unclear and a dictionary definition for the term cannot be found and "nonhaving" is not defined in the specification.

Regarding claim 17, it is unclear whether the paramagnetic particles are bound to non-magnetic microparticles. Claim 17 recites "the non-magnetic microparticles" in lines 1-2 of the claim. There is insufficient antecedent basis for this limitation in the claims.

Claim Rejections - 35 USC § 102

4. Claims 15-17 are rejected under 35 U.S.C. 102(b) as being anticipated by Liberti et al. (US 6,013,532).

Liberti et al. teach a composition comprising optimized, pre-coated (coated with molecules that are physically absorbed to the paramagnetic core, col. 6, lines 7-12) paramagnetic particles bound to non-magnetic particles having a detectable fluorescent label (particles comprise paramagnetic material, col. 6, lines 7-12; magnetic particles which can be substituted with paramagnetic particles are bound to cells, col. 12, lines 35-58), the paramagnetic particles having an average diameter of 0.2 μm or less (col. 5, line 65 – col. 6, line 7), which is less than the average diameter of the particles having a detectable fluorescent label with a size of 10 μm (col. 7, lines 58-62), which falls within the recited range of an average size from about 1 to about 20 μm. Although Liberti et al. fail to specifically teach paramagnetic particles pretreated with paraformaldehyde, such a limitation is drawn to a method of making particles and it is unclear what further product limitations are provided by pretreatment with paraformaldehyde. Since all product limitations are taught by Liberti et al. the composition is capable of being pre-treated with paraformaldehyde.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

The factual inquiries set forth in *Graham* **v.** *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

5. Claims 1-11 are rejected under 35 U.S.C. 103(a) as being unpatentable over Kausch et al. (US 5,665,582).

Regarding claims 1-5, Kausch et al. teach a composition for the detection of one or more target entities present at low concentrations (col. 43, lines 46-54) in a mixture, the composition comprising: non-magnetic microparticles operably linked with a first binding partner (col. 11, line 65 – col. 12, line 1) bound to a complementary second binding partner (col. 16, line 66-col. 17, line 5), said binding partner being operably linked to optimized, paramagnetic particles (magnetic beads can also be paramagnetic beads, col. 6, lines 24-26; second binding partner is streptavidin, col. 18, lines 54-57) smaller than the average size of the non-magnetic particles (col. 12, lines 1-6), wherein the non-magnetic microparticles are either unlabeled (col. 13, line 62 – col. 14, line 10; col. 18, lines 57-61) or detectably labeled (biological material is anchored to non-magnetic material which is detectably labeled with binding composition, col. 16, lines 66-67; col. 15, lines 4-10; col. 18, lines 57-61), wherein the paramagnetic particles bear free binding sites distal to the surface of the non-magnetic microparticles (magnetic particles can be

substituted with paramagnetic particles, and magnetic particles are anchored to a surface and distally bound to human chromosomes, col. 18, lines 54-64) having a streptavidin binding capacity (magnetic particles can be substituted with paramagnetic particles which are coupled with streptavidin, col. 18, lines 54-56) and wherein the bound paramagnetic particles are bound to a first binding partner of a free form first binding partner (paramagnetic particles bound to human chromosomes, col. 18, lines 54-64). Although the paramagnetic particles of Kausch et al. are not specifically taught as being pre-coated, the particles are coated with a material for non-specific binding before binding occurs (col. 24, lines 3-5). Kausch et al. teach the first binding partner being biotin (between the microbead and the cell, col. 14, lines 6-10; between the magnetic particle and the cell, col. 18, lines 54-57) and the complementary binding partner being an avidin species (avidin coated magnetic particles, col. 18, lines 54-57). Kausch et al. teach 2.5 ng/ml Fe_3O_4 (col. 42, lines 55-64), fail to teach a streptavidin binding capacity from about 1 to 10 nmoles biotin/mg iron.

However, it has long been settled to be no more than routine experimentation for one of ordinary skill in the art to discover an optimum value for a result effective variable. "[W]here the general conditions of a claim are disclosed in the prior art, it is not inventive to discover the optimum of workable ranges by routine experimentation" Application of Aller, 220 F.2d 454, 456, 105 USPQ 233, 235-236 (C.C.P.A. 1955). "No invention is involved in discovering optimum ranges of a process by routine experimentation." Id. at 458, 105 USPQ at 236-237. The "discovery of an optimum value of a result effective variable in a known process is ordinarily within the skill of the art." Since applicant has not disclosed that the specific limitations recited in instant claim 1 is for any particular purpose or solve any stated problem,

and the prior art teaches that the amount of streptavidin can be varied in order to adjust to the concentration of biotin labeled chloroplasts (col. 43, lines 46-54), absent unexpected results, it would have been obvious for one of ordinary skill to discover the optimum workable ranges of the methods disclosed by the prior art by normal optimization procedures know in the streptavidin binding art.

With respect to claims 6-11, Kausch et al. teach free binding sites on the layer of pre-coated paramagnetic particles that are capable of indirectly binding at least three additional entities (binding occurs sequentially, so simultaneous binding occurs after all entities are bound, col. 21, lines 12-25). The additional entities are selected from the group consisting of: one or more target specific third binding partners, being an oligonucleotide probe complementary to a oligonucleotide sequence or an antibody, operably linked to said first binding partner (col. 17, lines 44-47; col. 23, lines 41-42; col. 34, lines 20-35); a fluorescent compound linked to the first binding partner (col. 6, lines 16-36; col. 8, lines 9-11; col. 18, lines 54-64; col. 20, lines 29-32); a biotin species with affinity for blocking residual binding sites on the second binding partner located on the paramagnetic particles (col. 24, lines 3-13); and a detectably labeled target specific fourth binding partner capable of recognizing epitopes on target entities different from those recognized by the third binding partner (a nucleic acid probe is specific to proteins; col. 18, lines 7-10).

Response to Arguments

6. Previous rejection of claim 1 under 35 USC 112, second paragraph has been withdrawn.

7. Applicant's arguments and amendments, see pages 2-3, filed 9 May 2005, with respect to the rejection(s)of claim(s) 1 under 35 USC 102(b) have been fully considered and are persuasive.

Therefore, the rejection has been withdrawn. However, upon further consideration, a new ground(s) of rejection is made in view of applicant's amendment requiring a streptavidin binding capacity from about 1 to 10 nmoles biotin/mg iron. Applicant argues Kausch et al. fail to teach paramagnetic particles that permit simultaneous enrichment and measurement of multiple specific target entities without non-specific interference. However this limitation is not recited in the rejected claims. Although the claims are interpreted in light of the specification, limitations from the specification are not read into the claims. See *In re Van Geuns*, 988 F.2d 1181, 26 USPQ2d 1057 (Fed. Cir. 1993). Applicant also argues the paramagnetic particles of Kausch et al. fail to permit magnetic enrichment at very low concentrations in a sample. However, it is unclear what concentrations are encompassed by very low concentrations and Kausch et al. teach paramagnetic particles for the detection of entities at low concentrations at column 43, lines 46-54.

8. Regarding claims 15-17, in response to applicant's argument that the references fail to show certain features of applicant's invention, it is noted that the features upon which applicant relies (i.e., magnetic particles crosslinked with paraformaldehyde) are not recited in the rejected claim(s). Although the claims are interpreted in light of the specification, limitations from the specification are not read into the claims. See *In re Van Geuns*, 988 F.2d 1181, 26 USPQ2d 1057 (Fed. Cir. 1993). Rejected claim 15 fails to recite a magnetic particle with paraformaldehyde on the outer surface. It is noted claim 15 recites a paramagnetic particle that is pre-treated with paraformaldehyde. However, as discussed above, it is unclear what product limitations are provided by a pretreatment with paraformaldehyde. Since the required product

limitations are taught by Liberti et al. the paramagnetic particles of Liberti et al. would be capable of pre-treatment with paraformaldehyde.

Conclusion

No claims are allowed.

9. Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Melanie Yu whose telephone number is (571) 272-2933. The examiner can normally be reached on M-F 8:30-5.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Long Le can be reached on (571) 272-0823. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

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7/15/05